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EDITORIAL

POST-GRADUATE STUDY.

The question of post-graduate study arises in every student's mind. It is the recognized, advisable course to take at least some training as an interne, no matter into what field of medical endeavour one is contemplating entering. One may dismiss this question with no further discussion.

However, the student who wishes to take some special training in a special branch of medicine or to advance his knowledge of general medicine still further, is faced with the question of "how to do it." The article by Dr. Hager Hetherington printed herewith discusses the problem of post-graduate study in Great Britain most helpfully from the practical standpoint. The various worrysome details of "spending a year in England" are dealt with to enable one who is contemplating such a trip to do so with the least difficulty. We believe that there will be many who will welcome such helpful pointers from one who has "been through it."

This all leads one to consider the question of post-graduate study in general. With the present-day keen competition in the medical profession and the modern tendency toward specialization, it is almost a necessity for one

to enlarge upon his education in an undergraduate medical school.

There are two types of medical men for whom it is necessary to enlarge their medical education—the specialist and the general practitioner who wishes to have a comprehensive idea of all branches of medicine. It is obvious from Dr. Hetherington's article that many such facilities are available in Great Britain.

There is one great feature, however, which must be considered—the financial problem. One may discuss at great length concerning the advantages of post-graduate study, but practically, one must always be mindful of and is indeed usually faced with the problem of financial support necessary for the successful attainment of these advantages. It seems unfortunate that a student's acquirement of medical knowledge should be limited by his monetary facilities, but such is the case. The solution of this problem, of course, is up to the individual—and to the conscientious student this problem often gives but transient difficulty. In many of these cases there is found an optimistic source of loan, in which some person is willing to pin his hopes upon the student's future.

OSLER'S IDEALS.

The following extract from Sir William Osler's writings puts forward the "Great Physician's" ideals of life, certainly most worthy of emulation:

> "I have had three personal ideals. One to do the day's work well and not to bother about to-morrow. It has been urged that this is not a satisfactory ideal. It is; and there is not one which the student can carry with him into practice with greater effect. To it, more than anything else, I owe whatever success I have had—to this power of settling down to the day's work and trying to do it to the best of one's ability and letting the future take care of itself
>
> "The second ideal has been to act the Golden Rule, as far as in me lay, toward my professional brethren and toward the patients committed to my care.
>
> "And the third has been to cultivate such a measure of equanimity as would enable me to bear success with humility, the affection of my friends without pride, and to be ready when the day of sorrow and grief came to meet it with courage befitting a man."

FACILITIES FOR POST-GRADUATE STUDIES IN GREAT BRITAIN

HAGER HETHRINGTON, B.A., M.B., M.R.C.P., London.

For the past few years there has been an increasing number of post-graduate students from this country seeking further knowledge and experience in the medical schools and hospitals of Great Britain. The medical schools of Edinburgh and London are numerous and widely scattered, and one can waste valuable time and money in search for the desired teaching. For that reason it occurred to the writer that as detailed information as possible regarding the facilities for post-graduate study in Great Britain would be of some value to the prospective student.

In the first place, the post-graduate student should decide whether he is going to limit himself to purely clinical and academic studies, or whether he intends to combine these studies with a period of practical work in a British hospital. This decision will depend upon the length of time he is able to stay in Great Britain, and his financial backing. If a visit of a few months to a year is contemplated, a hospital appointment would be a hindrance. But if he intends to make his stay indefinite, especially if its duration depends upon the acquisition of funds while there, a hospital appointment is very desirable

If the decision has been made in favour of seeking a hospital appointment, the student should try the Dominion Council examinations. The possession of this diploma enables one to register in any Province of Canada, a very important consideration for anyone contemplating post-graduate work in Great Britain. Of course, any graduate of a British University can try the licensing examinations for Great Britain. But this is expensive, and would take considerable time to accomplish.

In December, 1927, Ontario and Great Britain discontinued their reciprocity agreement for license to practise. Since that time it has been necessary for any physician registered in Ontario to first register in a Province which has reciprocity with Great Britain before registration in that country is possible. This may be done either by trying the licensing exams of the Province concerned, or by writing the Dominion Council examinations and then applying for registration in that Province. The latter course is by far the more practicable. The Provinces still having reciprocity with Great Britain and the fee in each case are: Nova Scotia, $50; Prince Edward Island, $50; Alberta, $65; Manitoba, $100. The application should be addressed to the licensing board at the capital of each Province concerned. The business can be transacted more expeditiously and cheaply before leaving this country, and its completion will save many heart-burnings on the other side. For registration in Great Britain, a licence to practise in the approved Province and a graduate certificate from a recognized medical school must be presented. It is also advisable, but not essential, to have a copy of one's birth certificate.

Registration of physicians in Great Britain is controlled by the General Council of Medical Education and Registration of Great Britain. The offices are situated at 44 Hallam Street, Portland Place, W.C., 1, conveniently near Oxford Circus. The fee for registration is five pounds one shilling. This fee suffices for all time, and would allow one to practice medicine without further expense on a subsequent visit to Great Britain.

The above decisions and arrangements having been made, the next

thing to decide is when and how to reach there. Here again there are several possibilities. For purposes of post-graduate study, it is useless to be in London until the schools are open in the fall. But in Edinburgh, courses in both medicine and surgery are given by the University of Edinburgh in the summer months. In London most of the post-graduate courses start in the fall. Unless travel for pleasure is contemplated, the best time to leave for the Old Country is in September. However, if travel in Great Britain is being considered, it is best to undertake it upon arrival, before attention to work or lack of funds make such travel difficult or impossible. As at least half the value of a journey to Great Britain is in the things seen and people met apart from the academic work, such travel is of distinct benefit. The manner in which the student reaches Great Britain will depend partly upon his financial backing and partly upon his ingenuity, and it is not a part of this article to discuss such methods.

To the uninitiated, the first few days in London may prove expensive For that reason, the following information may be of value. It is not always possible to obtain rooms at some of the more centrally located hotels with moderate rates, such as the Strand and Regent Palace Hotels. But there are several other hotels where rooms, with or without board, may be had fairly reasonably. Of the first type is the White Hall chain of hotels scattered over the West End and through Bloomsbury. Of the second type, there are many good hotels, of which may be mentioned the Imperial on Southampton Row and the Royal on Woburn Place.

For the first few days in London the student may live at these places while deciding upon the courses to be taken, and looking about for more permanent quarters. With regard to the latter decision, there are several important considerations, viz., location, cost, and companionship. To consider the last question first, the student may prefer to live with his travelling companions. In that case a boarding house where he can get breakast and dinner should be sought. These may be found in profusion scattered through Bloomsbury and other parts of London. It is usually fairly easy to find one within reasonable distance of any of the medical schools. On the other hand, the student may prefer to live in a club with other students There are several where reasonable board may be obtained. Of these, Connaught Hall, Torrington Place, was originally intended for Canadian students, but it now offers accommodation to all students from the Dominions and Colonies. The rates are about three guineas weekly for room and board. It is quite close to University College Medical School and Hospital. A more recently established club is London House, in Caroline Street, off Guilford Street. Students must be introduced by two members of the club, and have testimonials from their banker or other responsible party. This is a very excellent place at which to live. The rates are under three guineas a week for room and board. Both these clubs have hot and cold showers, which are difficult to find in the older hotels of London. Other clubs for bachelors, not necessarily students, are to be found in various parts of London. Of these may be mentioned the Caledonian Christian Club on Endsleigh Street, W.C., 1., and the Tavistock Residential Club, on Tavistock Square in the same district.

Several of the London medical schools give post-graduate courses in general medicine and surgery each year, St. Bartholomew's, Guy's, London and King's College being among the most important. Most of the other hospitals maintain teaching clinics in the out-patient departments, and some have courses in special subjects. All these facilities are available to post-graduate students. To enrol in any of the courses the applicant may either write to the Dean or Secretary of the medical

school concerned, or see either of those officials personally. Some of the courses are limited in number, and it is advisable to register early, either before leaving Canada or immediately upon arrival in London. This applies especially to the courses given by the larger teaching hospitals, as Bart's, Guy's, London, etc. Since the other courses are usually not limited in number, it is not necessary to register until the clinics or lectures begin.

The nature of the general surgical and medical courses given by the various medical schools naturally varies in detail, but the principle is the same. The courses of the London hospital may be taken as examples. The fall courses begin early in October, and run for ten weeks up to the Christmas season. Similar courses are given in the spring, beginning in April. In these courses the post-graduate students are limited to about 20 in number. These are entitled to full under-graduate teaching privileges, and may attend any under-graduate lecture as well as the post-graduate ones. Courses of lectures are given in the various branches of medicine, physiology, pathology, etc. The students are allowed the freedom of the wards and out-patients departments. Clinics are given by members of the teaching staff on patients examined by the students in both ward and out-patient departments. The surgical courses convey the same privileges to post-graduate students enrolled in them. Courses are given in various branches of surgery, physiology, pathology, anatomy, etc. There are practical courses given in anatomy and surgical anatomy. Surgical procedures are carried out in the anatomical laboratories.

In addition to these general courses, those who wish as well more intensive instruction in a particular branch of medicine or surgery, especially the former, may attend courses given by those hospitals which deal with these specialities. Such hospitals are the National Hospital for Diseases of the Heart, on Westmoreland Street; the National Hospital for the Treatment of Nervous Diseases and Epilepsy, in Queen Square; the Hospital for Sick Children, on Great Ormond Street; St. John's Hospital for Diseases of the Skin, in Leicester Square, etc. Each of these hospitals maintains an out-patient department where post-graduate instruction is given. As well, these hospitals give courses of instruction at various times throughout the year.

The National Heart Hospital has a two-weeks' course at least twice a year, in January and October. At this course lectures are given in the mornings by cardiologists from the various teaching hospitals. Ward clinics are held in the afternoon, at which the student may examine cases.

At Queen Square a course on various aspects of neurology is given twice a year, lasting about six weeks. As well, this hospital accepts post-graduate students as clinical clerks. This carries the privilege of examining ward patients, writing the hospital histories, and attending ward rounds and out-patient clinics.

St. John's Hospital gives a course in Dermatology twice a year, lasting several weeks. This consists of a course of lectures as well as attendance at out-patient clinics at five p.m. daily.

The Hospital for Sick Children does not offer a course of instruction, but attendance on ward rounds and in out-patient department where teaching clinics are held, with the privilege of examining patients, can be obtained.

Most of the teaching hospitals besides those already mentioned allow post-graduate students to attend the various clinics in the out-patient departments, where instruction is given. So any post-graduate student, if instruction in a certain branch of medicine or surgery is desired, can attend that particular clinic at the various hospitals.

The fees for the above courses vary from time to time. The longer general courses in medicine and surgery, such

as those at Bart's, Guy's and London Hospital, cost twenty to thirty guineas each. For the courses at the National Heart Hospital the fee is seven guineas. The course at Queen's Square costs six guineas. The fees for attending the various out-patient's and ward clinics differ with the hospital concerned, but average from one to two guineas per month.

As well as the above teaching facilities for which a fee is charged, there are some clinics and lectures which may be attended without cost. St. George's Hospital at Hyde Park corner maintains a teaching clinic in Neurology on Tuesdays at 5 p.m. which is extremely interesting and instructive. Guy's Hospital have a teaching clinic on Tuesdays at 2 p.m. in general medicine. The Post-Graduate Fellowship, 1 Wimpole Street, gives free courses of lectures at various times. The Royal Society of London, the London Medical Society, the Royal College of Surgeons and the Royal College of Physicians, have lectures at various times of the year, which are advertised in advance in the *Lancet* and *British Medical Journal*. These are held either at 5 p.m. or in the evening, and do not interfere with other academic or clinical work. It is rarely that a week passes without an interesting lecture or series of lectures being given.

For those who wish to study pathology apart from a general course, ample opportunities are present. At each teaching hospital there are daily post-mortem examinations at which instruction is given. These hospitals also maintain excellent pathological museums where many profitable hours may be spent. There is also the museum of the Royal College of Surgeons in Lincoln's Inn Field, off Kingsway, which is without a peer in the number and interest of its specimens. Except for the last-mentioned museum, a small fee of about a guinea a month is charged by the medical school concerned.

London is unique in the possession of a scientific lending library. This is a private enterprise run by the publishing house of Lewis, situated on Gower Street, near University College Hospital. Here books may be rented at the rate of about five shillings for three months, and as many as wanted may be taken on payment of a small deposit. Subscriptions may be renewed at the end of the three months as often as desired. Hence it is not necessary to carry many books overseas. Each of the medical schools has an excellent library which is available to the post-graduate students taking work in those hospitals. As well, the Royal College of Surgeons Library in Lincoln's Inn Field is available, upon introduction, to all post graduate students. Books may not be removed, but may be read from ten a.m. till six p.m. It is an excellent place at which to study.

If the student intends to stay a year or more, it is well to join the Royal Society of Medicine or the British Medical Association. The former is situated at 1 Wimpole Street and the latter in Tavistock Square. The fees, for the former about five guineas and the latter two guineas, entitle the member to use the library and attend meetings as well as a year's subscription to the Journals of the Society.

The selection of the post-graduate course to be taken will, of course, depend upon the time, finances and interests of the individual. The time taken up by the courses will vary considerably with the different schools. The course at the London Hospital, for instance, occupies every other day fully from 10 a.m. until 6 p.m., the alternate days being free. The course at Guy's Hospital occupies every day from 10 a.m. until about 3 p.m. The course at Queen's Square fills every afternoon from 2 p.m. until about 5 p.m., leaving the morning vacant. At the Heart Hospital the course fills the whole day every day; its out-patient's clinics are held in the mornings. The course at St. John's is from to 6 p.m. The out-patient clinics and the ward

rounds at Gt. Ormond St. are in the morning, those at Queen's Square are in the afternoon. Most teaching hospitals have out-patient clinics both morning and afternoon. At all hospitals operations are performed in the afternoon. By much juggling of time-tables it is possible to fill the day as fully as desired with lectures, clinics, or study in pathological museums. But there are some things to watch. The work should be confined to adjacent hospitals on one day. They will save time and money in travelling from one clinic to another. It is remarkable how many unnecessary miles can be traversed during a day unless the time table is carefully planned. The larger medical schools maintain lunch rooms at which meals may be obtained more cheaply than outside and with a minimum loss of time.

The facilites for post-graduate study in Edinburgh are extremely good and the student should try to spend a part of his time at that centre. It is impossible to give in detail the various courses available in Medicine and Surgery and this information may be obtained by writing to the Registrar of the Royal College of Physicians of Edinburgh or the Secretary of University at Edinburgh.

The method of registration for those who wish to take a hospital appointment in Great Britain has been given. Before leaving the country such students should be supplied with three written testimonials as to their experience and character. It is wise to have several signed copies of each, since they are required to be forwarded with all applications for hospital appointments.

In London itself there are three types of hospitals. The teaching hospitals are usually not available for appointments, such being filled from the affiliated medical school. The smaller teaching and non-teaching hospitals have appointments available every six months. These appointments are for work on a single branch of surgery or medicine and are non-rotating in character. However, the short time of service allows students to hold two appointments in a year. The London County Council hospitals have positions available from time to time for locum tenens or permanent appointments. Outside of London there are numerous appointments which are not difficult to obtain, but these take the students away from the teaching centres. There is usually a remuneration attached to all appointments at the rate of about 60 to 80 pounds a year. All these hospitals advertise in the British Medical Journal and the Lancet, where the desired position should be sought.

This spring the British Parliament has approved plans for the development of a post-graduate hospital in the west end of London. It is expected that it will be functioning in a year or two, but its presence will not likely interfere with the courses outlined above.

While the above account does not pretend to give the complete facilities for post-graduate studies in Great Britain, it is hoped that it will prove useful to the student who is contemplating study there and perhaps may lead some wavering spirit to make the journey, which is well worth while. The writer takes this opportunity to thank his associates who have helped him to gather the above information.

THE INCIDENCE AND PATHOLOGY OF ESSENTIAL HYPERTENSION*

By W. J. HENDRY, B.A., '33.

In recent years the attention of the medical profession and of the laity has been directed to the subject of high blood pressure, its meaning, cause, effect and prognosis.

Definition.

To Sir Clifford Allbutt we owe the definition of hyperpiesia or essential hypertension as it is more generally known on this continent. This condition he described as one of which a permanently raised blood pressure is the dominating feature, associated with left ventricular hypertrophy, terminating usually in heart failure and sometimes in cerebral haemorrhage with little or no evidence of renal inefficiency. The definition excludes renal disease in any of its forms.

In practice, the terms hypertension and its synonyms hypertonia and hyperpiesia are rather loosely used. The view advanced by Volhard that alteration of the peripheral resistance to the blood flow on the basis of widespread functional or structural vascular change is now recognised as the predominant factor in heightened arterial pressure. Of course, the efficiency of the myocardium to provide dynamic energy is granted, but this factor, along with those of blood mass, viscosity and velocity are generally relegated to a position of minor importance.

The traditional division of hypertension into the primary simple or essential type on the one hand, and the so-called secondary type on the other is invalidated by the acceptance of the point of view that elevation or arterial pressure is the result of arteriolar activity. Pal states (1925) definitely that, with few exceptions, all hypertension becomes a manifestation of vasoconstriction excessive in degree or extent.

Normal Limits.

Before one may discuss high blood pressure, the normal values must be defined. As with all other physiological figures there is considerable variation from one individual case to another. The outside limits of the adult normal systolic blood pressure reading are one hundred and five millimetres of mercury at the lower end of our scale and one hundred and forty-five millimetres as the upper limit. The great majority of adults fall in the range of one hundred and ten to one hundred and thirty millimetres, but the wider limits are those usually considered as bounding normality. Undoubtedly blood pressure increases slightly with increasing age, but such rough and ready rules giving the blood pressure as age plus one hundred millimetres, and so on, give utterly fallacious results. On the average, too, the systolic blood pressure in women is lower than that in men by ten millimetres of mercury.

The diastolic pressure, a measure of the peripheral resistance to the circulating blood, is from thirty-five to fifty millimetres of mercury less than the systolic pressure in the same individual. Ninety-five millimetres of mercury is usually considered as the maximum value of a diastolic pressure still remaining within normal bounds.

Incidence.

How prevalent is this disease or sign, whichever one may call hyper-

*A paper delivered before the Toronto Chapter of Alpha Omega Alpha Honorary Medical Fraternity, March 20, 1933.

tension? The sources of information in these cases are the records of the life insurance companies. Of 146,992 individuals, presumably healthy in all other respects, there were 2,568 cases of hypertension seen by the examiners of the New England Mutual Life insurance company from 1919 to 1924, an incidence of 1.74 per cent. A comparable figure, 1.6 per cent., is given by the Metropolitan Life Insurance Company of New York. In about half a million applicants, there were eight thousand persons with a systolic blood pressure in excess of one hundred and forty millimetres of mercury. The condition is not one of but passing interest!

Age Incidence.

Essential hypertension may occur at any age. It is occasionally present in children and it is not uncommon in young adults. It begins most frequently, however, between the ages of forty and fifty. Janeway's statistics show that 80-90 per cent. of his cases accurred between the fortieth and sixty-ninth years. It appears, therefore, that it is a disease frequently beginning at the age of forty, and continuing from that time on the blood pressure rising slightly year after year. In the cases cited by Kernahan, Anderson and Keith the average age was forty-seven years.

Sex Incidence.

"It is extremely difficult to decide whether essential hypertension is more prevalent in the male or the female sex," states H. O. Mosenthal. Much stress has been placed lately on the fact that it is likely to occur in women at the time of the menopause. However, on this subject the authorities are hopelessly divided. On the whole, the opinion is that in dispensary practice the disease is more common in women than in men. In private practice the opposite seems to hold true, although in neither instance is the preponderance of one seen over the other very noticeable.

Incidence in Native Races.

A comparison of the incidence of hypertension amongst members of our Western civilization and members of more primitive native races is most interesting. In the African negro tribes of Kenya Colony near the shores of Lake Victoria Nyanza there was not a single case of hypertension in 1,800 admissions to the Mission Hospital. In the laboring classes of native Egyptians Ismail found hypertension to be very rare. Among some four thousand patients in the medical wards of a certain Chinese hospital, J. H. Foster found but one instance of Essential hypertension. This patient was a Chinese nurse, a woman of nervous temperament whose education was completed in America and who returned to China with the habits and attitudes of a Westerner.

The systolic pressure of occidentals residing in China was found to be lower than it had been in America. Similarly in the tropics it is found that the blood pressure of white men is ten to fifteen millimetres of mercury lower than it had been in the temperate zone.

We shall leave the queston of incidence of essential hypertension to consider the pathological changes seen in this condition. Time does not permit us to cite cases and analyse their findings. We must, therefore, refer to the literature on the subject and we shall consider first the changes in the arterioles.

Changes in the Arterioles.

It is only natural that, in a condition primarily of vascular nature, one should look for pathology in some part of the circulatory system. The arterioles which form the chief partion of the peripheral resistance to the circulatory blood now claim our attention. The work of Landis and others has shown the arterioles to be vessels of from forty to fifty microns in diameter. All the vessels to be considered in the subsequent paragraphs, arterioles and

smallest arteries, measure from twenty-five to one hundred microns. These dimensions include the vessels of the retina as well as the afferent vessel to the kidney glomerules.

A. M. Fishberg examined the arterioles in some seventy-two cases of essential hypertension coming to autopsy. Invariably lesions of the terminal arterioles were present. These lesions consisted of a deposit of hyaline material under the endothelium in a rather irregular manner. In many ceses there was hyperplasia of the internal elastic membrane with the formation of multiple lamellae, a finding similar to that described by Jores. These changes this author refers to as arteriolosclerosis.

In every one of the cases did the vasa afferentia et interlobulares of the kidney show the lesions. The arterioles of other organs were less frequently attacked, spleen in about two-thirds of the cases, pancreas in about one half, liver in less than one-third, and the brain in about one-fifth. The lesions in these organs were not so marked as those in kidney.

Arterioles of the skin, skeletal muscles, myocardium, lungs, gastro-intestinal tract and thyroid were very rarely involved. In such cases the changes were minimal in amount.

Fishberg comments on the difference in distribution of the arteriolosclerosis and the atherosclerosis seen in the large vessels. The site of predilection of the latter is the larger vessels, aorta, then brain and extremities. Arteriolosclerosis is commonest in kidney, spleen and pancreas

Fishberg's findings definitely lead to the conclusion that the view that hypertension is due to the statically increased resistance offered by organic lesions of the arterioles in untenable. There is, he finds, no time true generalised arteriolosclerosis such as would be required for the production of hypertension from this cause. Kernahan and his co-workers at the Mayo Clinic find evidence of changes in the vessels of skeletal muscles, as well as in the organs referred to by Fishberg. They state "The frequent absence of any lesion in the arterioles of voluntary muscles obtained at necropsy in cases of essential hypertension as reported by Jores, Fahr, Evans and Fishberg seem best explained by the fact that their series, perhaps, did not include cases of the serious progressive type of hypertension such as we have classed as cases of early malignant or malignant hypertension."

Returning to Fishberg's conclusions, he remarks that changes in the arterioles of a nature similar to the arteriolosclerosis of essential hypertension occur naturally with advancing years. This is particularly true in the spleen, a fact emphasized also by the Bell and Clawson. Fishberg states "Arteriolosclerosis is a pathological exaggeration of these physiological changes, resulting from the increased wear and tear incidental to the hypertension." "On the whole, the renal changes," says this author, "cannot be reconciled with the theory that essential hypertension is due to a disorder of renal function."

In their studies, Kernahan, Anderson and Keith recognize three types of so-called essential hypertension. First is benign hypertension in which there may be no lesions in the peripheral arterioles, or the lesions there may be moderate in degree. The findings are quite in keeping with the retention of adequate retinal, cardiac and renal function accompanied by no change in or slow progression of the general condition.

The second group is that of severe benign or early malignant hypertension. The blood pressure is usually higher and the complete clinical picture is more severe. The pathological findings in the peripheral arterioles are correspondingly more marked. In many cases retinal, cardiac and renal function is adequate.

Lastly is malignant hypertension. Here is seen a definite type of retinitis and cardiac enlargement. Early dis-

turbances of cardiac and renal function are more often present than in either of the other two groups. While the blood pressure is generally markedly raised this feature is not essential to the syndrome as the other factors may be marked while the blood pressure is but moderately increased. In these cases of malignant hypertension there is almost invariably a marked thickening of the wall and narrowing of the lumen of the arteriole in skeletal muscles. The clinical course is rapidly progressive to a fatal termination. "In other words, there are good reasons for considering malignant hypertension as the terminal stage of the severe benign or early malignant type. We have seen cases which undoubtedly belong to the benign group, but which at a later date present the classic features of the malignant type. Thus there is clinical and pathologic evidence in certain instances at least that the basic lesion in the three groups is one of degree. On the other hand, we recognize that in the great majority of cases of benign hypertension, the malignant syndrome never develops."

The arteriolar lesions seen most commonly were hypertropny of the medial coat of these small vessels. Proliferation of the intima was also seen frequently. The lumen of the arteriole is frequently partially occluded, and the ratio of the lumen to the wall is altered. Normally, the thickness of the arteriolar wall bears a relation to the lumen of one to two. In the cases of group two, advanced benign or early malignant hypertension, the ratio is altered to that of one to one point four, and in the cases of malignant hypertension, to the ratio of one to one point one.

These investigators state further that there were no signs that the changes were degenerative or similar to those of senile retrogression. The widespread distribution of the arteriolar lesions in many viscera as well as in the muscles is claimed to be indicative of diffuse vascular disease.

Kernahan, Anderson and Keith conclude by stating that the presence or absence of the arteriolar lesions in the muscles is of value in diagnosis and prognosis of the individual cases. They state "the type of lesions suggests hypertrophy in the face of excessive strain. One interpretation would be that the lesion is secondary to the hypertension. However, these are cases of malignant hypertension in which there is only a moderate rise in blood pressure. This might indicate that the diffuse involvement of the arterioles is primary and that sustained hypertension might result on account of increased peripheral resistance."

Murphy and Grill, in sixteen cases of malignant hypertension, confirm the findings of the Mayo clinic workers. Throughout this series, cardiac hypertrophy was seen. In the gross, the kidneys of these cases presented variable pictures, they varied from small, contracted granular organs to large, smooth viscera, the large kidneys of subacute (the clinical subchronic) nephritis. On microscopic examination the smallest arteries and the arterioles (size from forty to one hundred and twenty microns diameter) of kidney, spleen, pancreas, liver and brain, were almost universally involved. There was definite intimal thickening together with hyperplastic changes in the internal elastic laminae and proliferation of the intimal connective tissue. Some cases showed hypertrophy of the media. Changes in the arterioles of skeletal muscles were also noted. These lesions were similar to those in the arterioles of other viscera.

In a series of four hundred and twenty cases of primary or essential hypertension, Bell and Clawson found renal arteriolosclerotic changes similar to those described above in over ninety per cent. of their cases. They have no definite figures for the changes in the arterioles outside the kidney, but their impression is that the other organs are involved in about the same proportions as those quoted by Fishberg. These

authors point out that in those cases dying from renal insufficiency, the degree of the renal arteriolosclerosis is greater than in cases dying a cardiac or cerebral death.

In his most recent publication (July, 1932) Murphy and his collaborators adopt a classification of hypertension quite parallel that of Kernahan, Anderson and Keith. In Murphy's group II. lesions in the arterioles of skeletal muscles were found in fifty-seven of three hundred and three cases. These arteriolar changes were moderately advanced in degree. In group III. malignant hypertension, the changes in the arterioles of skeletal muscles were constantly found.

From the arteriolar lesions we turn to that part of the cardiovascular system providing the dynamic energy necessary for an efficient circulation, the myocardium.

Changes in the Heart.

In 1924 Bell and Hartzell published the results of their investigations on the weights of the normal heart. They found the average weight of two thousand hearts with cases of hypertension excluded to be two hundred and eighty grams for females and three hundred and thirty grams for males. They claim it is very seldom a male heart exceeds four hundred and fifty grams or a female heart four hundred grams.

In their later publication, 1928, Bell and Clawson use the weight of the heart as a means at autopsy by which they diagnose hypertension during life, should such a diagnosis be necessary. They use as their criterion of hypertension a heart with a definite left ventricular hypertrophy not associated with any of the diseases known to cause hypertrophy. A hypertrophied heart is considered as one weighing four hundred and fifty grams in females and five hundred grams in males.

Hadfield and Garrod give an excellent description of the cardiac changes. 'The typical heart of essential hypertension shows hypertrophy of the left ventricle with or without associated dilatation. In the absence of dilatation, the thickened walls with massive papillary muscles and a septum bulging somewhat to the right enclose a small conical cavity in which any increase in size is due to lengthening rather than broadening. The increase in bulk of the muscle is due to a greater thickness of the individual fibres and not to an increase in their number.''

Of the heart weights in the three hundred and seventy-five cases of Murphy and his collaborators, a word

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Practical Hematological Diagnosis by O. H. Perry Pepper, M.D., Professor of Clinical Medicine, and David L. Farley, M.D., Associate in Medicine, University of Pennsylvania. Octavo of 562 pages, with 3 inserts in colors. $7.00.

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DEALERS IN GOOD BOOKS SINCE 1885.

might be said. Only eighteen per cent. were normal weight, forty-seven per cent. weighed from four hundred to six hundred grams and seventeen, or four point five per cent. weighed from eight hundred to one thousand grams. The greatest proportions of the heavier weight hearts were found in cases of malignant hypertension. In this group no hearts are classed as of normal weight.

The third region of the body worthy of consideration in this paper is the retina

Retinal Changes.

In hypertensive disease the retinal changes are strikingly characteristic and of great value both in diagnosis and prognosis.

From the pathological standpoint several factors claim our attention. The first is sclerosis of the retinal vessels. These vessels are arterioles when they are considered from the standpoints of size and structure. The changes seen in these vascular channels are similar to the lesions of renal arterioles. Their walls are thickened with proliferation of the intima and also with hyaline change in the wall. Comparison of figures quoted by O'Hare and Walker for the degree of sclerosis of retinal vessels in hypertensive and non hypertensive patients is interesting. In the non-hypertensive group eighty-two per cent. had normal vessels or showed questionable sclerosis, as opposed to the hypertensive group who showed but two per cent. with this slight degree of change. The most severe degrees of sclerosis were seen exclusively in the hypertensive group.

The second feature is the so-called exudate, giving the white spots in the retina in benign forms and cotton-wool patches in malignant hypertension. The term exudate is a misnomer, for the spots represent not exudates but areas of degeneration in the retina. The more sharply outlined shiny spots of the benign hypertension cases are areas of fatty degeneration. Their stellate appearance in certain cases is said to be due to the distribution of the retinal connective tissue in the neighbourhood.

Retinal haemorrhages are often seen. They may be single or multiple, large or small, superficial or deep, and may be with or without relation to the larger vessels.

Papilloedema is a characteristic finding in malignant hypertension. It may reach a degree of six dioptres. Some cases of hypertensive disease have been reported in which this was the only finding, and the whole picture very closely simulates one of intracranial tumour.

Changes in the Renal Glomerulus.

In 1930 Leone McGregor of Boston published a report of his findings of changes in the renal glomerulus in cases of hypertension These are, he claims, as typical as the arteriolar lesion. The change consists of a decrease in size and a simplification of the glomerulus accompanied by a marked thickening and wrinkling of the glomerular basement membrane. In his series of fifty-one cases the average per cent. of such glomeruli is forty-seven in the renal group (as regards the type of death), thirty-three in the cardiac group and twenty-four in the cerebral group. McGregor states further that the arteriolosclerosis precedes, and is related to the change in the glomerular basement membrane. It is stated that a hypertensive contracted glomerulus may be seen in a normal kidney in rare instances.

Summary.

In this paper we have shown that essential hypertension is seen in from one to two per cent. of otherwise healthy persons. It is a disease of later adult life, most commonly, and affects the sexes in about equal numbers. The condition is practically unknown in less highly civilized peoples.

The chief lesion is a change in the

arterioles, in the viscera and in the skeletal muscles in the more severe forms. The changes seen most frequently are (1) hyaline changes in the intima, (2) proliferation of the internal elastic lamina, (3) hypertrophy of the media.

Cardiac hypertrophy of a left ventricular type is generally well marked. Retinal changes include arteriolosclerosis, fatty degeneration of the retina, haemorrhages and papilloedema. In the kidney simplification of the glomeruli with a thickened, wrinkled glomerular basement membrane may be seen.

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ESSENTIAL HYPERTENSION*

By R. B. KERR, B.A., '33.

A. Known physiological factors controlling Blood Pressure.

1. *Nervous Factors*:

(a) Bainbridge Reflex.—This is a mechanism which increases blood pressure by increasing the output of the heart. When the pressure in the veins is increased a reflex passes up the vagus to the vagus centre which inhibits the vagus and this decreases the output of the heart.

(b) Marie's Reflex—when the pressure is raised in the arch of the aorta, the aorta is stretched which causes a reflex to pass up the depressor portion of the vagus which tends to slow the heart and decrease the pressure. There is also a reflex through the vosomotor centre causing a dilation of the arterioles.

(c) Carotid sinus mechanism: (i) If blood pressure falls in carotid artery impulses pass from the carotid body which (a) increase rate of heart, due to decrease in vagus impulse; (b) constrict peripheral arterioles by acting through the vaso-motor centre; (c) increase secretion of adrenalin by acting through the sympathetic system. (ii) If the blood pressure rises in the

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carotid artery (a) vagus impulses slow heart rate; (b) the impulses to the arterioles decrease and the arterioles dilate.

2. *Chemical Factors*:

Adrenalin—small amounts lower B. P. by dilating capillaries, and larger quantities contract arterioles and blood pressure rises.

Vasopressin or pitressin—causes increase in blood pressure—are liberated by the posterior pituitary

Sympathin—liberated at sympathetic endings causes an increase in blood pressure.

Acetylcholine—dilates arterioles—is liberated at parasympathetic ending in arterioles—lowers blood pressure, also liberated in heart causing decrease in rate.

Histamine—liberated at sensory nerve endings following antidromic impulses—dilates capillaries.

Adenylic acid—liberated in damaged tissues—dilates capillaries.

B. Contributory factors to the causation of essential Hypertension.

1. *Heredity.*—That heredity plays a most important role in essential hypertension there can be no doubt. Christian mentions 40 cases of which only two showed a negative family history.

The person who has a tendency to develop hypertension most usually is the well-known type who is delicate in youth, as he grows into adult life he puts on considerable weight, improves in his general health. This is the type who become intensive, ambitious workers, expending great quantities of mental energy, he is the man who becomes successful. Success brings worries and responsibilities. He is too busy for exercise or for relaxation. He eats heartily, and does not care for too much exertion. If he takes up a hobby he "works at it" rather than plays. He is a large, stout man with the familiar ruddy plethoric complexion. Contrasting with this type is another type—usually females—who are pale, thin, undernourished, nervous, and with evidence of non-fertility.

The person with this hereditary tendency shows early evidences of vasomotor instability which will be referred to again. It is this instability of the autonomic nervous system which is the hereditary factor according to Geger.

Obesity.—The association between obesity and hypertension has been stressed by many. Fisk has shown that in those who were 20% or more overweight, 78% had hypertension. Figures even higher than his have been given by some. There must be some connection between obesity and hypertension, its exact nature is not clear Geger suggests that obesity, hypertension and diabetes are all expressions of an underlying abnormality of metabolism. This while it is very vague seems to be a more reasonable suggestion than that obesity in itself is an etiological factor of hypertension.

Psychic factors.—Probably the most important extraneous etiological factor in hypertension is that of the response of the vascular system to psychic stimuli. Many have commented upon the effect of mental strain in the causation of hypertension. Lord Dawson of Penn has shown that in school children prior to examinations there is an increase in blood pressure; Stocks and Karn have demonstrated that school boys in schools with strict discipline have a higher average blood pressure than those in easy-going schools. Many individual cases have been reported in which the psychic factor plays an important part—one notable case was that of a man who showed a blood pressure of 280 mm. while in hospital. It was discovered that he was worried about his home and not being able to see his wife; whereupon it was arranged that his wife be brought from an outlying part to see him and almost immediately his pressure fell to 150 mm. This is, of course, an extreme case, but it empha-

sizes the effect of psychic factors. It has also been suggested that the rare finding of hypertension in Chinese and African natives is due to the unhurried life of these people. One example is that of a Chinese girl who came to America for her education and took over the habits and attitude of our civilization. She was the only person of 4,000 examined by Foster in China who had hypertension. One must consider the question of race and climate also in connection with this question.

There can be no doubt that this factor plays a most important part in the etiology of hypertension in a person with a tendency for the disease. The stress and strain of living, the struggle for existence, the anticipation of effort, and the desire to forestall, all play a great part in civilization which as Lord Dawson of Penn states, "show reactions with bodies and minds of a certain physiological cast."

Chemical Factors.—There have been many attempts to discover a chemical cause of essential hypertension. I will not endeavour to go into this fully. Of course the discovery of adrenalin caused many to believe that the cause of this condition was at hand. It has never been demonstrated that there is an increase of adrenalin in the blood stream in essential hypertension. It must be remembered, however, that emotional stimuli can cause a liberation of adrenalin—it would appear that the last word has not been said in this regard.

Many substances have been proposed which arise from nitrogen metabolism as being responsible for hypertension. Major's work with guanidine is the most outstanding of these, he demonstrated that in about 60% of cases of hypertension there was an increase in the guanidine content of the blood, also that injection of the substance experimentally increases the blood pressure, the arteriolar constriction produced could be followed by the ophthalnoscope. However, there is some question about the accuracy of the methods of determination of guanidine in the blood.

Westphal has demonstrated that the blood cholesterol is increased in 80% of hypertension patients. This substance experimentally appears to have a synergistic effect with adrenalin, increasing its activity.

There has been demonstrated also that some bacterial products have a constricting effect upon the arterioles. This opens up the possibility of foci of infection as a contributory factor in this condition.

In connection with dietary factors much work has been done to determine the effect of protein. Without going into the details of the discussion, it is fairly well accepted that the factor of protein in the diet has little or no effect upon the condition.

Menopause.—I placed this under a separate heading, not because it is considered by all as an important factor in hypertension, but because it is the subject of much controversy. Many have emphasized the fact that high blood pressure develops rapidly at the age of 40 in women—but this is also the age of incidence in men. There is a considerable argument as to whether or not myomata of the uterus are associated with hypertension. The only undisputed point is advanced by Alvarey and Zimmermann, who state that women with disorders of the sexual organs have a higher blood pressure than do normal women. However, I believe that we must leave this question of the menopause with no conclusions drawn as yet.

There is another subject about which there has been much controversy in the past, namely, whether or not arteriosclerosis is a cause of hypertension. An important contribution by Lange in 1928 has shown that these two conditions are antagonistic. He began with cases of "pure hypertension" and "pure senile arteriosclerosis" and showed that in the hypertensive group

there was a hyperexcitablity of the peripheral vessels whereas in arteriosclerosis there was a sluggish often subnormal reaction. This he considers is a fundamental difference, and believes that the two conditions arise in a different manner—hypertension is a functional disorder of the vasomotor system which is followed by arteriolosclerosis and arteriosclerosis is a senile change not connected in any way with hypertension.

Muller and Hubener have shown some facts which are of fundamental importance in connection with the direct cause of hypertension. They showed that in contrast to the orderly disposition of the small vessels in normal persons, there is an irregularity and lack of pattern in the structure of arterioles, capillaries and venules. The arteriole was abnormally contracted, the venous limb was abnormally dilated (giving the explanation of the plethoric complexion) and capillary flow was irregular with frequent stasis.

The work of Stopford and Telford in connection with arterial changes associated with cervical rib is very helpful in explaining some of the facts connected with hypertension. They suggest that the pressure of the cervical rib on the sympathetic nerves in the brachial plexus causes stimulation of these nerves. This stimulation causes vaso-construction phenomena in the hands with eventual change in the arterial wall. In this we have a means demonstrated whereby central stimulation may cause vasoconstriction with resultant change in the vessels.

Thus from this consideration of the etiological factors of hypertension it seems that we can focus our attention on the vasomotor system and on the small peripheral vessels of that system as the main factor in this condition. As in so many other general diseases there are two main factors: (1) heredity—we are born with a certain vasomotor makeup and vascular structure, and (2) contributory factors which attack hypersensitive vessels.

CLINICAL PICTURE.

(a) Symptoms and signs of Essential Hypertension—a permanently raised blood pressure may exist in the early stages, at least, with no symptoms whatever to the patient of any change in his physical condition. Many such cases are recorded in the literature and are seen every day by physicians.

However, sooner or later hypertension will manifest itself in an individual in whom it exists. This manifestation takes various forms, depending to a very great extent upon the make-up of the individual. In the early stages of the disease the clinical picture presents a rather bizarre picture of non-specific symptoms.

The onset of irritability, psychic instability or easy mental and physical fatigue often marks the beginning of the manifestations of hypertension. Janeway described the occurrence of dizziness, fullness or tightness in the head, and occipital headache in the early morning hours—wearing off toward noon as symptoms of early hypertension disease. Digestive disturbances very often constitute the first danger signal of nature—the abdomen may become distended and "indigestion" may be present—a feeling of fullness and discomfort following meals —with some feeling of "gas." Very often vague joint and muscle pains occur associated with hypertension, Kaufmann finding this complaint present in about 70% of cases—they have been described as due to spasm of blood vessels in these two locations. Haemorrhages are frequently seen in hypertensive individuals, especially from the nose, gastro-intestinal tract, uterus, kindney, and lungs. A loss of weight sometimes occurs in these cases also. The characteristic high colour of the hypertensive is very frequently present.

Among the signs of essential hypertension per se—the occurrence of increased blood pressure is, of course, the most outstanding. The definition

of the disease depends on this. The blood pressure shows different heights in different individuals. The systolic pressure may be anywhere from 140 or 150 mm. Hg. to over 300 mm. Hg. The diastolic pressure being 30 - 40 mm. less than these figures, the height of the diastolic pressure depending, however, upon the functional efficiency of the heart muscle and the condition of the arteries. It is probably not necessary to mention that care should be taken during the determination of the blood pressure not to excite the patient, but to rather distract his attention from the proceedings, so as to attempt to remove any phychic effect during the examination. The two factors which should be noted in examination of the blood pressure are its height and its variability. These are inversely related, that is, the higher the blood pressure the less variable it is. A high but variably blood pressure from day to day or month to month indicates an earlier stage of the disease and more hopeful outlook for treatment, while a high fixed blood pressure indicates that organic change has occurred and makes the prognosis less favourable. The level of blood pressure may be classed into three main groups—(a) those with an elevation of the systolic pressure and a normal diastolic pressure—this group represents about 52% of the causes of hypertension according to Frosst, and is made up of younger people with mild hypertension; (b) those with high systolic and high diastolic pressures, representing 44% of cases and consists of older patients with the disease more advanced, and (c) those with high diastolic pressure and relatively low systolic pressure—4%—occurring late in the disease and represents severe organic change. This represents the characteristic progress of hypertension.

Retinal changes: The changes in the retinal picture in essential hypertension has recently become a most important diagnostic method, and I believe that it would be well to go into this rather fully. At this point, only the retinal changes of benign hypertension will be described, those of malignant hypertension being left until later. We must remember that the vessels which we see in the retina are small vessels of the calibre of arterioles. O'Hara and Walker have quite definitely shown that there is a relationship between hypertension and retinal vessel changes, and that there is no relationship between general arteriosclerosis of the larger arteries and arteriolosclerosis of the retina. Moreover, they have discovered several cases with normal blood pressure at the time of examination and retinal arteriosclerosis, but with a history of previous hypertension.

In describing the retinal lesions we must first mention that there are some cases of hypertension about 15% which show no retinal change—it is reasonable to assume that these patients' hypertension is of short standing.

The changes seen in the retina in benign hypertension can be classed into four groups (1) arteriolar spasm which has been demonstrated not infrequently, (2) arteriolosclerosis—which is manifested by narrowing of the lumen of the vessel, the formation of the "white line" on the arteriole and the "copper wire arteriole" the arterio-venous constrictions, i.e., apparent constriction of the vein at the point of crossing of a vein and arteriole which actually is displacement of the vein to a deeper part of the retina by the thickened arteriole, tortuosity and irregularity (beading) of the vessels. (3) Haemorrhage—is considered by Lange as almost always indicating hypertension; trauma and blood dyscrasias being rare causes. (4) There are also changes in the retina which have been referred to by Fishberg and Oppenheimer as arteriosclerotic retinopathy. These when present are characterized by small white or ivory coloured spots which are sharply outlined and have a "hard" appear-

ance, there may also be some pigmentation of the retina.

Clinical Course.—O'Hare has made a division of the course of essential hypertension into three stages, division into which allows for a convenient discussion of this. The first or prehypertensive stage begins at birth and extends to 30-35 years. During this stage evidences of vascular instability begin to appear usually in the second decade—high colour, blushing, nervous instability, cold sweaty hands, and perhaps menorrhagia in the female. The second stage is entered upon sometime between the ages of 30 and 40 years, in which fluctuating rises of blood pressure occur, usually no symptoms are present, these cases are only discovered upon routine medical examinations. The third stage is begun from 3 to 10 years following this at 40 or 45 years of age, in which the blood pressure becomes permanent—it is in this stage that the patient first comes to the doctor complaining of various vague symptoms which have been outlined in the section of symptomatology.

Once hypertension is established the clinical course of the disease depends very greatly upon the extent of arterial damage in the varous organs, and the particular organ most involved. According to Mosenthal of 100 of hypertension 60 will die of cardiac disease, 20% cerebral disease and 10% of renal disease, the remaining 10 will die of some coincident disease.

(1) *Cardiac.*—The earliest evidence of the heart's response to hypertension is frequently to be seen in enlargement of the heart—seen on the orthodiagram as bulging of the upper border of the left ventricle. This is followed by enlargement of the shadow outward and downward. The aorta may respond to the increased blood pressure by dilation, elongation and displacement, best demonstrated by the oblique diameters during fluoroscopy. The upward displacement of the aorta may be demonstrated by an episternal pulsation. The apex beat is usually a heaving thrust and the aortic second sound is accentuated, provided these changes are not hidden by fat or emphysema.

The patient shows the usual progressive signs and symptoms of heart failure—about which I need not discuss at this time.

Accompanying the dilation of the heart, there is heard in many cases an apical systolic murmur, also rarely there may be aortic systolic and diastolic murmurs—care must be taken to differentiate these from those caused by syphilis, rheumatic fever, arteriosclerosis and anaemia.

Electrocardiographic examination offers no help until quite marked myocardial degeneration occurs.

As the heart shows more and more degenerative changes, departures from the normal rhythm occur. Premature beats occur frequently associated with hypertension, and are to be considered as serious in late hypertensive disease according to Geger. Auricular fibrillation and flutter occur Tochycardia is present in about one half of the patients. Pulsus alternans is a grave sign occurring late in the disease.

Angina pectoris and coronary thrombosis are not uncommon cardiac involvements met with in hypertensive patients.

(2) *Cerebral.*—Cerebral involvement to some extent occurs in many hypertensive patients. Headache or fullness in the head, is the most frequent symptom—occurring characteristically in the morning before rising and passing off before noon. Vertigo, tinnitus, drowsiness or sleepiness may occur. Pahl describes cases of evenescent attacks of muscular weakness and aphasia which he attributed to vascular spasm, but Allbutt has discredited this and believes these to be due to small haemorrhages or thromboses of small vessels. The outcome of cerebral involvement may result in two ways—cerebral degeneration of senility or an acute cerebral crisis—haemorrhage

or thrombosis with its accompanying nervous manifestations.

(3) *Renal.*—In every case of hypertension there are some renal changes, but the kidney can withstand many such insults without giving evidence of renal sufficiency. However, provided that the patient does not succumb to some other complication of hypertension, he will eventually show renal involvement. The first symptom occurs along with the presence of hyaline casts as the earliest evidences in the urinalysis of renal insufficiency. The two-hour test shows an increase in the night volume, and a decrease and fixation in the specific gravity. As the disease progresses these evidences of renal failure increase is severity. Blood chemistry shows increase in N.P.N. and urea. In the late stages of hypertensive renal disease a distinct pallour and anaemia develop. The fundus shows anaemia of the disc, marked papilloedema, cotton wool exudates, and occasionally the macular star, the vessels of course show marked sclerosis. The blood N.PN. rises, the urinary findings of albumen, casts (hyaline, granular, and waxy) increase and the patient dies in uraemia.

Mention should also be made of the fact that a not infrequent complication of hypertension is diabetes.

MALIGNANT HYPERTENSION.

Recently Keith, Wagener and Kernahan have described a clinical entity which they believe to warrant being separated from the disease essential hypertension. This condition ras been called by them malignant hypertension. This represents an advance in our understanding of the condition of hypertension. The average age of this condition is 42 years with the majority of patients between 33-35 years. The term malignant is appropriate because of the fact that the disease is so rapidly progressive, the patients living at the longest about 4 or 5 years. The blood pressure is high—systolic usually 220-280 and diastolic 120-190. The heart is enlarged in about 50% of cases and the aortic secand sound is accentuated in 75%. Impairment of vision is a frequent complaint along with the other symptoms of hypertension.

The retinal examination is the important diagnostic feature of these cases. This has been divided into four stages:

(1) Hyperaemia and mild oedema of the disc and retina about the disc, few superficial haemorrhages and cotton wool exudates.

(2) Oedema spreading to macular area and to the periphery, numerous haemorrhages and cotton wool patches.

(3) Oedema recedes from the periphery and small areas of pigment are seen, punctuate exudates appear, and form irregular stars in the macula, marked arteriolosclerosis is present.

(4) Pale disc, blurring and increase of glial tissue, perivascular thickening is seen along the vessels, occasional haemorrhages and atrophy of the retina.

The course of the disease is rapidly progressive. The type of death is either cardiac, renal, cerebral or a combination of any of these failures. The progress of the failure of these organs is most rapid-developing in many cases within one year.

PROGNOSIS.

(a) Benign Hypertension.

The prognosis of benign hypertension has been altered considerably recently by life insurance figures. It has been shown that an increase by 10 mm. of the blood pressure over normal causes an increase in 36% in the mortality or a decrease of 10 years is expected and an increase of 50 mm. or more increases the mortality by 314% or a decrease of 25 years in expected life.

It must be remembered, however, that while these figures are valuable from an insurance standpoint, they do not necessarily mean a great deal in an individual case.

The diastolic pressure is a better

means of prognosis than the systolic pressure. Hamman states that all patients with diastolic pressure of 110 mm. and over will die in 10 years.

This prognosis appears rather dark, but the literature is thickly sprinkled with many individual cases of hypertensives living for many years with high blood pressures, and also one must stress that the prognosis is considerably altered by the institution of treatment.

(b) Malignant Hypertension.

This condition, however, presents a fairly definite and uniformly bad prognosis. 90% of the cases died within 4 years and the majority within 2 years of the onset of symptoms.

DIAGNOSIS.

Benign Hypertension.

The diagnosis of this condition depends of course upon the ruling out of other causes of hypertension; some of these I will mention:

(a) *Constitutional Hypertension*—there have been described persons in whom there was a rise in pressure over the accepted normal. This, however, is constant and does not show signs of progression. The only method of differentiating this from essential hypertension is by observation over a period of time.

(b) *Chronic Nephritis.*—Some cases of hypertension with considerable renal damage may show a picture which would be confused with a chronic glomerula-nephritis. There are a few points which may aid in the diagnosis between these conditions, the vascular changes are less marked in nephritis, the blood pressure in nephritis is rarely above 200 mm. The fundus changes of chronic nephritis show anaemic discs, dense retinal oedema, whereas hypertensive renal disease shows hyperaemic discs, sclerosis of vessels, and less dense oedema with cotton wool exudates. The differentiation is of little practical value, as patients with either of these pictures have almost similar kidneys functionally and are open to similar dangers

(c) *Hyperthyroidism*: Hyperthyroidism is accompanied by increased blood pressure. This characteristically, however, is an increased systolic pressure with normal diastolic pressure. Also the history of heat intolerance, the tremor, the exopthalmus if present and an increased B.M.R. are important differentiating points.

(d) *Congenital heart disease* may be associated with hypertension. Other signs of congenital heart disease such as cyanosis, murmur, will help to clear up this diagnosis.

(e) *Suprarenal tumour.*—This condition occurs rarely and is responsible for the elevation of blood pressure. The characteristic of this condition are paroxysms of hypertension which last a few minutes or hours.

(f) *Polycythaemia hypertonica*—is a very rare cause of hypertension. This is associated with an increase in red cells, the cause of the increased blood pressure, however, is not known.

The diagnosis of malignant hypertension depends upon the rapidity of the course of the disease, the lack of anaemia, and most important, the retinal picture described above. The only conditions with which it may be confused are benign essential hypertension and chronic glomerulonephritis. The former can be differentiated by the course of the disease and the retinal changes and the degree of hypertension. The latter by the occurrence of anaemia in chronic nephritis and lack of it in malignant hypertension and the retinal changes. In malignant hypertension the oedema of the retina is less dense, there is less tendency for snowbank formation, and there is a hyperaemia of the disc.

TREATMENT.

(a) General. The chief success in the treatment of this condition lies in its early discovery. There is some hope of at least slowing the progress of the

disease if treatment is begun in the early stages before severe vascular damage has occurred.

The treatment requires full co-operation between physician and patient. The patient should be told somewhat of his condition, so that he will understand how he can help in its treatment.

Success in treatment has been reported in cases where the patient has been able to live a more carefree life than formerly. He must attempt to either protect himself from the various psychic shocks which have troubled him formerly, or he must accept a more calm and philosophical existence.

A change in environment, in the form of a long holiday, with freedom from responsibility, has often done much to alleviate the condition.

Complete rest in bed for short periods is advocated by some, notably Elliott, who suggests one to two weeks in bed with absolute freedom from business four times a year.

Moderate exercise is advocated as a good measure; walking, golf, horseback riding, are of a satisfactory type. These not only provide exercise, but a complete diversion for the patients.

While this is the ideal treatment, it must be realized that in practice it falls far short of the ideal, since much depends upon the co-operation of the patient.

b. **Diet.** The question of diet has undergone considerable change in the recent past. The old idea that protein foods should be decreased in hypertensives is losing favour in the light of modern investigation. Most believe that it is desirable to decrease overweight by a limited calory diet, and that the diet should be limited in quantity rather than quality.

Allen has suggested a salt-free diet for hypertension. There is, however, much controversy concerning the benefit of this method, except, of course, in cases with renal failure.

So far in the discussion of treatment the main idea to be brought out is moderation in all things — moderation in work, exercise, and food.

c. **Drugs.** Drugs play an important part in the treatment of hypertension, supplementing the above measures. Sedatives, such as bromides and luminal, are very good in an attempt to decrease the avtivities of the patient.

Vasodilators of many kinds have been advocated — and it is still of doubt as to whether or not they are of much value. I believe that we may say that some vasodilators may be of value in the early stages of the disease before severe organic lesions in the vessels have occurred. The effect of the nitrates is rather transient and not of much permanent value. One drug which may prove to be of value is sodium sulphocyanate. This was introduced by Westphal on the theory that it dissolved cholesterol, which they believed was a factor in the causation of hypertension. This drug in large doses produced some toxic effects, but if given in small doses there is no toxicity. It has been shown that sodium sulphocyanate is present in the blood, urine and saliva of normal individuals Small doses from 0.2 to 5 gr. t.i.d. have a quiet marked effect of decreasing the blood pressure. It appears, however, that if the pressure is decreased in some individuals with advanced vessel lesions untoward effects are produced which disappear after removal of the drug — apparently the patient needs the increased pressure to carry on.

Of course, symptoms arising out of complications of hypertension must be treated as they arise.

In conclusion, it has been pointed out that the disease essential hypertension is now considered to be one due to a functional upset of the vasomotor system, originally, upon which is superimposed vascular lesions in various organs of the body. The further understanding of the condition and its more intelligent treatment depends upon a more thorough knowledge of its pathological physiology.

AN ENZYME ATTACKING THE TYPE III. PNEUMOCOCCUS

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The purpose of this article is to present a summary of the recent work of Dubos, Avery and Goodner. The papers reviewed (1-6) have appeared during the past three years.

Recent work on the pneumococcus has shown that the type specificity of types I, II. and III., is closely related to polysaccharides existing in the gummy capsule surrounding the organism. An individual polysaccharide of a distinctive chemical structure has been demonstrated to exist for each of the three types. The polysaccharides are referred to as "specific soluble substances" or "type-specific polysaccharides." For the sake of brevity the substance from, for example, the type III pneumococcus is sometimes referred to as "S-III."

For some time Dubos, Avery and their co-workers at the Rockfeller Institute have been searching for an enzyme which would attack the pneumococcus polysaccharides. Their purpose in doing so were threefold:

(i) The fact that the capsular polysaccharides are the substances responsible for type specificity is shown by disappearance of their immunological specificity on acid hydrolysis. This disappearance takes place at a rate parallel with the hydrolysis of the polysaccharide as measured by its breakdown into reducing sugars. However, an objection might be raised that this rather drastic treatment destroyed a hypothetical impurity which was the real thing responsible for type specificity. To dispose of this objection, an enzyme was sought which split specifically the polysaccharide. Then, reasoned the investigators, if the immunological properties of the capsular preparation disappear at the same rate as the enzymic breakdown of the polysaccharide, it is the polysaccharide itself that is responsible for these properties. An enzyme would be too specific to break down an accompanying impurity.

(ii) Toenniessen had found that when B. vulgarus was grown in company with the Friedländer bacillus, the latter organism grew without producing its capsule. Dubos and Avery wished to see if a bacterium could be found which would produce a similar effect upon the pneumococcus.

(iii.) Finally, and most obviously of all, the therapeutic potentialities of an enzyme attacking the pneumococcus are very important.

Enzymes splitting polysaccharides and simpler carbohydrates were tested. Cultures of various molds, yeasts, soil actinomycetes, and bacteria known to split cellulose were tried. All were ineffective. Next, the investigators turned to the organisms multiplying in localities where hemicelluloses accumulate, since the specific soluble substances have many of the properties of the hemicelluloses. Among the materials tried were leaf mold, composts, barnyard manure, and soils, such as peat. which are rich in organic matter. From a New Jersey cranberry bog was isolated an organism capable of splitting S-III. It was named the S-III bacillus. S-III is a polymer of an aldobionic acid, which consists of two hexose radicals one of which carries a COOH group.

The culture medium used was one containing, as the sole source of organic carbon, S-III in concentrations of from .001% to 0.2%. The reason this was used was that many organisms produce certain enzymes as **starvation**

phenomena. The results amply justified this step, for, as we shall see, the organism only produces the enzyme splitting S-III when this polysaccharide is the sole source of organic carbon. Further, the medium immediately eliminated by death from starvation all the useless organisms. Lastly, it was desired to produce a material as free as possible from proteolytic activity, and hence the use was indicated of a medium free from proteins or their products of hydrolysis.

The S-III bacillus proved to be pleomorphic, motile, spore-forming, variable in gram-staining according to medium on which it is grown, strictly aerobic, non-gas-forming, inhibited by glucose but growing in certain other sugars. It was extraordinarily specific for S-III, having no effect on the following substances: S-I and S-II; the polysaccharides of types A, B and C of the Friendländer bacillus; the polysaccharide of type "a" of **Hemophilus influenzae**; and gum arabic. The last-mentioned substance simulates S-III in the precipitin reaction. Hence we apparently have here an example of an enzyme showing **greater specificity than an immune reaction.**

Properties of the Soluble Enzyme Extracted from the Bacterial Cells.

The bacillus is a strict aerobe, but the enzyme produced from it by autolysis and filtration works anaerobically even in the absence of a hydrogen acceptor. The enzyme is unaffected in its action by the presence of normal serum. It is inactivated at 60°-65°; it is an endocellular enzyme, and bears a quantitative relation to substrate decomposition.

When added to a suspension of type III pneumococci, the enzyme removes their capsules without destroying the cocci themselves. Indeed, it does not affect their power of regenerating their capsules when transferred to a medium free from the enzyme. The capsule is the means of protection of the pneumococcus against phagocytosis. A therapeutic possibility for the enzyme is thus immediately suggested.

In Vivo Experiments.

0.1 cc. of a preparation of the enzyme protected mice against the effect of 10^5 times the fatal dose of a virulent culture of type III. pneumococcus, both being administered intraperitoneally. It remained in effective concentration in the body for from 24 to 48 hours. Heating it to 70° for ten minutes destroyed the subsequent in vivo action of the enzyme. A preparation showing weak action in vitro also showed weak action in vivo.

The enzyme also showed curative action when administered to mice twelve to eighteen hours after inoculating with one hundred times the minimum fatal amount of a culture of type III pneumococcus. Microscopic examination of the peritoneal exudates of these animals revealed the fact that the protective action of the enzyme was due to removal of the capsule and phagocytosis by the polymorphonuclear leucocytes. This affords an interesting contrast to the action of antibodies, which also prepare the pneumococcus for phagocytosis, but do so by specific sensitization. This alters the capsular material but does not strip it off.

Yield of the Enzyme.

No appreciable amount of the enzyme is formed by the S-III bacillus in absence of S-III in the culture medium. Notwithstanding this, the organism grows far more freely in other media, such as peptone solution.

The yield of the enzyme is greatest when the level of S-III in the medium is 0.1%. Concentrations of 0.4% and above inhibit completely the growth of the bacillus. This may be attributed to toxicity of S-III, but Dubos prefers another explanation. He thinks it may be due to autolysis of the organism and consequent release of the enzyme into the medium. This results in destruction of the S-III by the free enzyme, which deprives the bacillus of its source

of energy and consequently causes a cessation of growth.

To bring light on this point, he tried to speed up the growth of the organism and simultaneously to depress its autolysis. It was found that if yeast extract was added to the medium, enzyme production was greatly increased, and at the same time cell autolysis and sporulation were arrested.

The yield of enzyme was also greatly increased by making growth conditions more aerobic, i.e., growing in shallow layers of medium. The yield was better at 30° than at either 37° or room temperature. Growth for seven to fourteen days before extraction improved the yield.

Several methods were tried for concentration of the enzyme. The only two found advantageous were vacuum distillation and ultrafiltration.

Toxic Effects of the Enzyme.

When yeast extract was added to the culture medium the enzyme proved toxic to mice. Reduction of the amount of yeast extract to 0.03% greatly decreased the toxicity while still increasing the growth of the bacillus. The use of toluene in the process of preparation was also found to produce marked toxicity and was discontinued.

The residual toxicity could be in a great measure removed by a few minutes contact with alumina gel C of Willstätter. Longer contact with absorbent irreversibly absorbed the enzyme itself.

Protective Action On Rabbits.

Rabbits were injected intradermally with a virulent culture of pneumococcus type III. This provides a less accessible type of infection than that produced in the mice which received an intraperitoneal injection. The usual result of such an infection is to produce death in from three to four days. Treatment by injection of the enzyme caused recovery from the disease; eighteen out of nineteen treated rabbits surviving, while two out of thirty-eight untreated rabbits survived.

No active immunity was produced after prompt recovery following enzyme therapy. However, if the treatment consisted of multiple injections of small enzyme, a high degree of active resistance to subsequent infection was elicited. This difference was thought to be due to the specific antigen being destroyed too early in the first-mentioned instance to permit of its functioning as an effective stimulus to antibody formation.

No discussion of the possibility of the formation of an anti-enzyme was given.

The amount of the enzyme necessary to cure the disease was proportional to the bacteremia count, i.e., to the amount of substrate present within the body. At the same time, recovery must also be dependent upon powers of phacocytosis.

Further news of work in this interesting new field is awaited with interest. Naturally, one hopes that news will appear of successful treatment of human patients, and perhaps of the isolation of enzymes which will attack the types I and II of the pneumococcus.

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INFLAMMATORY DISEASE OF THE GALL BLADDER

By A. RAXLEN, B.A., '34.

AETIOLOGY OF CHOLECYSTITIS.

A. **Predisposing Causes.**
1. Calculi.
2. Foreign bodies — worms, hydatids, etc.
3. Factors favouring biliary obstruction and stasis.
   (a) Sedentary habits.
   (b) Obesity.
   (c) Abnormal tumors.
   (d) Pregnancy.
   (e) Tight lacing.
   (f) Interference with the movements of the diaphragm.

B. **Direct Causes.**
1. Infection.
   (a) Generalized blood infection —Typhoid, etc.
   (b) Focal—tonsil, teeth, etc.
   (c) Alimentary disease — duodenal catarrh, inflammatory of liver, appendicitis, oral sepsis.
2. Interference with blood supply.
   (a) Torsion.
   (b) Infarction.

ROUTE OF INFECTION.

Controversy has raged for some time over this point. Rosenow and Wilkie favour the blood route. Magner believes that infection in most cases spreads via the portal circulation to the liver and thence to the gall-bladder by lymphatics. The organism is probably a streptococcus. Occasionally B. coli or B. Typhosus are the culprits.

R. R. Graham some years ago pointed out the fact that biliary disease was one of a large group of upper gastro-intestinal disturbances marked by a somewhat common symptomatology. These are usually designated by the patient as stomach trouble. The group comprises the following:

(1) Gastric ulcer.
(2) Gastric carcinoma.
(3) Duodenal ulcer.
(4) Duodenal ileus — 3 types.
   (a) Due to visceroptosis—pull of the superior mesenteric artery.
   (b) Due to ligament of Treitz.
   (c) Due to Harris membrane.
(5) Biliary disease.
(6) Migrain.
(7) Functional nervous indigestion.

In all these conditions we find a disturbance of gastric function, either motor or secretory. The reason for this community of symptoms apparently lies in the common sympathetic innervation, which permits reflex disturbances at a site, often far removed from the site of mischief. In discussing biliary disease, one has to take this group into account and attempt to differentiate the lesion causing the disturbance. R. R. Graham also pointed out that there are three stages in the development and progression of cholecystic disease.

(1) Reflex Stage—During which the symptoms are referred to the stomach.
(2) Stage 2—During which the symptoms are referred to the gall-bladder area.
(3) Stage 3—The stage of tragedies—marked by complications such as common duct obstruction, acute cholecystitis, acute haemorrhagic, pancreatitis, perforation, etc.

Operation during the first stage shows a mortality of 1—2% as opposed to a mortality of 10—25% in the third stage. The first stage marks the beginning of chronic cholectystitis, which

usually progresses to the second and third stages, unless adequately treated.

CHRONIC CHOLECYSTITIS.

Pathology.—Obviously the picture depends on the extent of the process, length of time, and other factors. Frequently the gall bladder is found to be filled with tenacious thick mucus, but may contain clear liquid bile. Calculi may be present. The mucosa often shows varying degrees of inflammation, with chronic cellular infiltration. On the other hand, the gall bladder may be of the so-called atrophic sclerosing type with stones, many adhesions, and calcified atrophic walls. Other forms are the chronic ulcerative type of chronic empyema. The bile in most cases is pale and unconcentrated. Another form of chronic gall-bladder is the strawberry gall-bladder or cholesterosis of the gall-bladder, characterized by large deposits of cholesterol in the mucosa.

Clinical Features—As a rule the patient complains of symptoms referable to the stomach.

(1) Sense of weight and fullness in the epigastrium after meals.
(2) Flatulent distention, relieved by belching and vomiting.
(3) Heart burn.
(4) Fat intolerance.
(5) There may be, in addition, occasional bouts of colicky pain, which may double him up, and there may be tenderness over the gall-bladder.

Of these features, closely akin to those seen in the other members of the group, previously described, we are compelled to make a diagnosis, which in most cases leads to a serious surgical operation.

Differential Diagnosis—The history is of extreme importance in the differentiation.

(1) Cholecystic disease is a long-drawn out disease, not characterized by remissions. The patient suffers from a continuous disability over many years.

(2) The distress bears no relation to the time of day, but is brought on by taking of food.

DUODENAL ULCER.

Here the history is characterized by:

(1) Remissions, periods of good health. Patient often knows in advance when he is going to be sick.
(2) Duodenal ulcer distress is characterized by the so-called triple rhythm—food, comfort, pain; the pain persisting until food is taken. Eventually a point may be reached in the history where the pain has become continuous, because the ulcer has penetrated into a near-by organ.

GASTRIC ULCER.

Gastric ulcer gives a more bazarre picture and a different rhythm. The position of the ulcer is important. An ulcer near the cardia, the least sensitive portion of the stomach, may produce no symptoms; whereas an ulcer near the pylorus, the common site, produces severe symptoms. The early stage of gastric ulcer shows the rhythm of food — comfort — pain — comfort. In other words, the patient is comfortable before he takes food, whereas with duodenal ulcer the patient has discomfort before he takes food. Continuous discomfort may be produced by penetration.

DUODENAL ILEUS.

(1) **Due to Superior Mesenteric Artery**—This is seen in visceroptotic individuals with protuberant lower abdomen. The individual gives a history of gradual development of symptoms. The position of the patient varies the position of his mobile caecum. Hence his symptoms are very variable in time and severity, depending on his position. There is no relation to food.

(2) **Due to Ligament of Treitz**—When the obstruction is due to this cause the symptoms are continuous and

progressive, resembling duodenal ulcer but lacking periodicity. Barium plate shows the dilated duodenum with the obstruction in the mid-line in the case of superior mesenteric artery obstruction and to the left of the mid-line in the case of the ligament of Treitz.

(3) **Obstruction due to Harris Membrane**—This membrane arises from the hepatic flexure and passes over the caput of the duodenum to the gastro-hepatic membrane. The pull of the colon, in severe constipation, tightens the membrane and produces obstruction. Relief from constipation and recumbency clears up the symptoms.

GASTRIC CARCINOMA.

Decreased acidity or achlorhydria are not necessarily diagnostic of carcinoma, and may be found in cholecystitis and other conditions. Possibly loss of appetite and imperfect emptying due to atony of the gastric muscle may be the first signs. Loss of weight, loss of energy, and anaemia of unexplained origin are warning signals. Once suspected, barium studies should be carefully carried out.

Migraine—This is a condition characterized by severe headache, with marked gastric upset — nausea, vomiting, etc., which clears up completely after a few hours' sleep.

FUNCTIONAL OR NERVOUS INDIGESTION

—is a rare, vague condition, which one should not diagnose until other causes have been carefully eliminated.

Diagnosis of Chronic Cholecystitis.

Besides the history and symptomatology, we have the following methods:

(1) *Duodenal Intubation.*

With examination of bile contents, chemically and bacteriologically. This method of Lyons, at one time extensively employed, has somewhat fallen into the discard.

(2) *X-Ray Studies.*

(a) Flat plate for gall-stones.

(b) Indirect X-ray studies following barium meal to determine distortion of neighbouring organs by adhesions.

(c) Cholecystography — This consists of X-ray studies following administration of sodium iodo phenolphthalein orally or intravenously This material is secreted into the gall-bladder where, if it is concentrated, it becomes visible as a dense shadow under X-ray. This method shows the failure of gall-bladder to concentrate, a disturbance, which may be only functional, or due to chronic disease. Obstruction of the bile ducts can also be demonstrated.

ACUTE CHOLECYSTITIS.

This most frequently follows chronic inflammation of the gall-bladder, but may be acute from the start.

The aetiology is therefore that of chronic cholecystitis, with some precipitatory factor superadded. This precipitating factor is often obstructed by a stone, adhesion, torsion, blow. Injudicious over-eating and exposure to cold are said to favour the onset of an acute attack.

Pathology—is variable, and several forms have been described.

Acute catarrhal form is common, we find.

(1) Tense gall-bladder with soft oedematous walls.

(2) Acute inflammation of the wall, infiltration of polymorphs and lymphocytes.

(3) Peritoneal covering is inflamed and often adherent to neighbouring organs by a plastic exudate.

(4) Neighbouring glands are swollen.

(5) Cystic duct is swollen and oedematous, with the lumen often occluded.

(6) Liver and pancreas often shows signs of inflammation.

Clinical Features.

In a typical case we may find:

(1) Local, paroxysmal pain or continuous pain if serous coat is involved.
(2) Tenderness in right upper quadrant.
(3) Rigidity.
(4) Pain may be referred to shoulder. This usually means extension of the inflammation to the diaphragm, or pain may be referred to appendix area. However, there is a dissociation of pain and tenderness which differentiates it from true appendicitis.
(5) Cutaneous hyperaesthesia over gall-bladder area.
(6) Jerky respirations, very frequently.
(7) Palpable mass sometimes, if gall-bladder is distended to any extent.
(8) Local peritonitis may result, with onset of reflex vomiting. This usually clears up without surgical intervention.
(9) Liver margin may be tender.
(10) Jaundice is not usually present unless ducts are also inamed.
(11) Severe inflammation and involvement of peritoneum will cause marked constitutional symptoms —fever, increased pulse, and leucocytosis.

Prognosis—is good. There is usually rapid subsidence of the attack with recurring attacks.

Sequelae—Hydrops or mucocele.
Empyema.
Chronic cholecystitis.
Adhesion to Colon, Pylorus, Duodenum, producing dyspepsia, Pyloric stenosis and dilatation of the stomach.

ACUTE SUPPURATIVE CHOLECYSTITES.

Pathology.—This is due to an acute suppurative inflammation, which may go on to ulceration and perforation. This form is frequently associated with gall-stones, which have the same relation to it, that fecoliths have to appendicitis. The peritoneal coat is usually a green or greenish black in colour. There may be adhesion to neighbouring intestine with obstruction. The wall of the gall-bladder is soft and friable. The mucous membrane is destroyed and may be replaced by granulations. The wall is densely infiltrated with leucocytes.

Clinical Features—are similar to those in the acute catarrhal form, but there is a much more marked constitutional disturbance with marked rise in temperature and pulse and marked leucocytosis. Vomiting and signs of intestinal obstruction may be present. The liver is often enlarged and tender.

ACUTE CANGRENOUS CHOLECYSTITIS.

This form is due to a virulent infection and occasionally to torsion or trauma. The attack may be precipitated by thrombosis, constriction of blood vessels, or obstruction of the cystic duct. This type is not common.

Pathology—The wall shows green or greenish black gangrenous patches and may be perforated. The vessels may be thrombosed.

Clinical Features—The constitutional symptoms are very marked. There is usually a very high leucocytosis.

The diagnosis is difficult, and immediate operation is desirable before perforation has taken place.

COMPLICATIONS.

(1) **Gastric Disturbances**—Gastric disturbances are not always reflex in nature. Adhesions to the duodenum or pylorus may produce similar disturbances. This is brought home by an analysis of the results produced by removal of the gall-bladder. Dwyer and Dowling obtained relatively complete disappearance of the symptoms in only 75% of a series of 300 cases.

(2) **Pancreatic Disturbances**—The digestive function of the pancreas is more often affected than the "insulin" function. However, Otto Ferger and other workers in Germany have shown the presence of decreased sugar tolerance in many cases of gall-bladder disease. Also in 10% cases Otto Ferger found a positive relationship between gall-bladder disease and the onset of diabetes mellitus. Deaver believes that the route of infection is via the lymphatics draining to the retro peritoneal glands near the pancreas. Acute pancreatitis is a very much more serious complication, but more infrequent. The route of infection here seems to be vit the natural passages, i.e., by regurgitation of bile up the pancreatic ducts.

(3) **Inflammation and Fibrosis of the Liver**—are often associated with gall-bladder disease, either as a cause or effect, probably both. These are some of the common complications. It is probable that the focal infection in the gall-bladder is also responsible in some cases for disturbances in distant organs such as the heart, kidney, etc. The effectiveness of any treatment will necessarily depend on the extent of these complications. These, in turn, depend on whether the treatment is early or late in the disease.

TREATMENT.

Chronic Cholecystitis.

Medical Treatment—

(1) Duodenal or oral administration of magnesium sulphate to stimulate emptying of the gall-bladder.

(2) Administration of bile salts to stimulate secretion of bile.

(3) Limitation of Diet—Also administration of high fat diets to stimulate the bile secretion has been suggested. The economic factor is also important in deciding upon surgical intervention.

Surgical Treatment—This is the ideal treatment in most cases. The earlier it is carried out the better are the results. Where this fails we are dealing with an extension of the inflammation beyond the gall-bladder, or in some cases stones may be missed in the hepatic or common ducts.

Treatment of Acute Cholecystitis.

This condition is not an emergency like acute appendicitis. The organ is more distensible and less liable to rupture. The usual course is to wait about 48 hours to give the condition a chance to subside. During this time local fomentations are applied. The patient is kept on a liquid nourishing diet, and fluids are administered paraenterally. If the condition does not show any improvement, then one is justified in operating and draining the gall-bladder. However, even if the gall-bladder ruptures, there is less chance of peritonitis than in rupture of the appendix. There is a marked tendency for adhesions to form between the colon, gall-bladder, mesentery, etc., thus walling off the infection. A local peritonitis is therefore often likely to result.

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